

What is claimed:

- 5           1.       A method of inhibiting entry of an infectious agent into a cell, comprising contacting a cell with one or more siRNAs which modulate expression or activity of a cellular gene and one or more siRNAs which modulate expression or activity of a gene or sequence of an infectious agent, thereby inhibiting entry of an infectious agent into a cell.
- 10           2.       A method of preventing infection in a subject comprising administering to the subject one or more siRNAs which modulate expression or activity of a cellular gene and one or more siRNAs which modulate expression or activity of a gene or sequence of an infectious agent, thereby preventing infection in a subject.
- 15           3.       A method of treating an infectious disease or disorder in a subject comprising administering to the subject one or more siRNAs which modulate expression or activity of a cellular gene and one or more siRNAs which modulate expression or activity of a gene or sequence of an infectious agent, thereby treating an infectious
- 20       disease or disorder in a subject.
4.       The method of any one of claims 1, 2, or 3, wherein expression or activity of a cellular gene and/or said gene or sequence of an infectious agent is inhibited.
- 25           5.       The method of any one of claims 1, 2, or 3, wherein at least one of said siRNAs is directed to a viral gene.
6.       The method of any one of claims 1, 2, or 3, wherein at least one of said siRNAs is directed to a chemokine receptor gene.
- 30           7.       The method of any one of claims 1, 2, or 3, wherein at least one of said siRNAs is directed to a chemokine receptor gene and at least one of said siRNAs is directed to a viral gene.

8. The method of any one of claim 5 or 7, wherein said viral gene is a p24 gene.
- 5 9. The method of any one of claim 6 or 7, wherein at least one of said siRNAs is directed to a chemokine receptor gene.
- 10 10. The method of any one of claims 2 or 3, wherein said siRNAs are administered intravenously.
- 11 11. The method of any one of claims 2 or 3, wherein said siRNAs are administered simultaneously.
- 15 12. The method of any one of claims 2 or 3, wherein said siRNAs are administered serially.
- 20 13. The method of any one of claims 2 or 3, wherein said siRNAs are mixed with a basic peptide prior to administration.
- 25 14. The method of any one of claims 2 or 3, wherein said siRNAs are encapsulated in liposomes prior to administration.
- 30 15. The method of any one of claims 2 or 3, wherein said siRNAs are topically administered to a mucosal membrane of the subject.
16. The method of any one of claims 2 or 3, wherein said siRNAs are administered once per week.
17. The method of any one of claims 2 or 3, wherein said siRNAs are administered once per every two weeks.
18. The method of any one of claims 2 or 3, wherein said siRNAs are administered once per every four weeks.

19. The method of one of claims 1, 2, or 3, wherein said infection is HIV infection.
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20. The method of claim 1, wherein said cell is a macrophage.
21. The method of claim 1, wherein said cell is a CD4<sup>+</sup> T cell.
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22. A composition comprising an RNA interference agent which inhibits expression of a chemokine receptor, or a fragment thereof.
23. The composition of claim 22, wherein said agent is an RNA which is homologous to a chemokine receptor, or a fragment thereof.
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24. The composition of claim 22, wherein said agent is an RNA which is homologous to a CCR5 gene, or a fragment thereof.
25. The composition of claim 22, wherein said agent is a double-stranded, short interfering RNA (siRNA).
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26. The composition of claim 25, wherein said siRNA is about 15 nucleotides to about 28 nucleotides in length.
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27. The composition of claim 25, wherein said siRNA is about 19 nucleotides to about 25 nucleotides in length.
28. The composition of claim 25, wherein said siRNA is about 21 nucleotides in length.
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29. The composition of claim 25, wherein said siRNA is double stranded and contains a 3' overhang on each strand.

30. The composition of claim 29, wherein said overhang comprises about 1 to about 6 nucleotides on each strand.

31. The composition of claim 29, wherein said overhang comprises about 2  
5 nucleotides on each strand.

32. The composition of claim 22, wherein said agent is a synthetic siRNA.

33. The composition of claim 25, wherein said first strand comprises the  
10 sequence of SEQ ID NO:1 and said second strand comprises the sequence of SEQ ID NO:2.

34. The composition of claim 25, wherein said siRNA is capable of inducing  
or regulating degradation of CCR5 mRNA.  
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35. The composition of claim 25, wherein said siRNA inactivates CCR5 by  
transcriptional silencing.

36. The composition of claim 22, further comprising a pharmaceutically  
20 acceptable carrier.

37. The composition of claim 25, further comprising a poly-G tail.

38. A vector comprising a short interfering RNA (siRNA) which is  
25 homologous to a chemokine receptor gene and is capable of promoting RNA interference of said a chemokine receptor gene.

39. The vector of claim 38, wherein said chemokine receptor gene is CCR5.

30 40. A vector comprising a DNA template which encodes an RNA which is homologous to a chemokine receptor gene and is capable of promoting RNA interference of said chemokine receptor gene.

41. The vector of claim 40, wherein said chemokine receptor gene is CCR5.
42. The vector of claim 40, wherein said vector is a lentiviral vector.
- 5 43. A cell transfected with the vector of claims 38 or 40.
44. A method of inhibiting gene expression of a chemokine receptor gene in a subject comprising administering to the subject an siRNA which inhibits gene expression of a chemokine receptor gene, thereby inhibiting gene expression of a  
10 chemokine receptor gene in the subject.
45. The method of claim 44, wherein said chemokine receptor gene is CCR5.
46. A method of preventing infection in a subject comprising administering  
15 to the subject an siRNA which modulates gene expression or activity of a chemokine receptor gene, thereby preventing infection in the subject.
47. The method of claim 46, further comprising administered to the subject an siRNA which modulates gene expression or activity of a gene or sequence of an  
20 infectious agent.
48. The method of claim 47, wherein said gene or sequence of an infectious agent is a viral gene or sequence.
- 25 49. The method of claim 46, wherein said infection is selected from the group consisting of: HIV, poliovirus, influenza, rhinovirus, Ebola virus, foot and mouth virus, papilloma virus infection, hepatitis, human papilloma virus (HPV), and herpes (HSV-2).
50. A method of treating an infection in a subject comprising administering  
30 to the subject an siRNA which modulates gene expression of a chemokine receptor gene, thereby inhibiting an infection in the subject.

51. The method of claim 50, further comprising administered to the subject an siRNA which modulates gene expression or activity of a gene or sequence of an infectious agent.

5 52. The method of claim 50, wherein said gene or sequence of an infectious agent is a viral gene or sequence.

53. The method of claim 50, wherein said infection is selected from the group consisting of: HIV, poliovirus, influenza, rhinovirus, Ebola virus, foot and mouth virus,  
10 papilloma virus infection, hepatitis, human papilloma virus (HPV), and herpes (HSV-2).

54. A method of modulating a CCR5-modulated immune response in a subject comprising administering an siRNA which modulates CCR5 gene expression to the subject, thereby modulating CCR5-modulated immune response in a subject.

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55. A method of inhibiting entry of an infectious agent into a cell expressing CCR5 comprising administering to the cell an siRNA which modulates CCR5 gene expression, thereby inhibiting entry of an infectious agent into the cell.

20 56. The method of claim 55, wherein said cell is a macrophage.

57. The method of any one of claims 44, 46, 50, or 54, wherein said subject is a human.

25 58. The method of any one of claims 44, 46, 50, or 54, wherein said siRNA is administered intravenously.

59. The method of any one of claims 44, 46, 50, or 54, wherein said siRNA is topically administered to a mucosal membrane of the subject.

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60. The method of any one of claims 44, 46, 50, or 54, wherein said siRNAs are mixed with a basic peptide prior to administration.

61. The method of any one of claims 44, 46, 50, or 54, wherein said siRNAs are encapsulated in liposomes prior to administration.